

Serial No.: 09/874,056
Supplemental Amendment

AMENDMENTS TO THE CLAIMS

1. - 14. (Canceled)

15. (New) An isolated protein consisting of the amino acid sequence set forth in SEQ ID NO: 4.

16. (New) A pharmaceutical composition, which comprises the protein of Claim 15 and one or more pharmaceutically acceptable additives.

17. (New) The pharmaceutical composition according to Claim 16, wherein said one or more pharmaceutically acceptable additives is selected from the group consisting of a pH regulator, a buffer, a stabilizer, and a preservative.

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18. (New) The pharmaceutical composition according to Claim 16, wherein said protein is in an amount of 1 pg to 1 g.

19. (New) The pharmaceutical composition according to Claim 16, wherein said composition is in a preparation form selected from the group consisting of an injection, an inhalant, a tablet, a granule, a powder, a capsule, and a suppository.

20. (New) A method for searching for an agonist or an antagonist of an insulin receptor-related receptor binding by the protein of Claim 15, comprising:
contacting said insulin receptor-related receptor with said protein in the presence of a test substance,

measuring inhibition of the binding in the presence of the test substance, and

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comparing binding of said protein in the presence of the test substance with binding of said protein in the absence of the test substance.

21. (New) The method according to claim 20, wherein said measuring is obtained by surface plasmon resonance.

22. (New) A method of regulating growth/differentiation in a cell which expresses an insulin receptor-related receptor comprising contacting said cell with the protein of Claim 15.

23. (New) The method according to Claim 22, wherein the cell is a cell related to a disease selected from the group consisting of diabetes, neuropathy, renal disorder, and gastrointestinal injury.

24. (New) The method according to Claim 23, wherein the cell is a pancreatic β cell.

25. (New) The method according to Claim 22, wherein the protein is contained in a culture supernatant of rat glioma cells stimulated with a phorbol ester and concentrated in a fraction eluted with 8-200 acetonitrile from a C18 reverse phase HPLC column.

26. (New) A method of regulating growth/differentiation in a cell which expresses an insulin receptor-related receptor comprising contacting said cell with the pharmaceutical composition of Claim 16.

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27. (New) The method according to Claim 26, wherein the cell is a cell related to a disease selected from the group consisting of diabetes, neuropathy, renal disorder, and gastrointestinal injury.

28. (New) The method according to Claim 27, wherein the cell is a pancreatic β cell.

29. (New) A method of treating a disease selected from the group consisting of diabetes, neuropathy, renal disorder, and gastrointestinal injury, comprising administering to a patient in need thereof an effective amount of the pharmaceutical composition of Claim 16.

30. (New) The method according to Claim 29, wherein said effective amount ranges from 1 pg to 1 g per day.

31. (New) An isolated protein or variant thereof, which has a binding activity to an insulin receptor-related receptor and the following characteristics:

- (a) it consists of the amino acid sequence of SEQ ID NO: 4
 - (b) it has a molecular weight of about 6135, 6206, 6250 or 6321 measured by mass spectrometry using the Fourier transformation ion cyclotron method.
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